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d hist

     (FILE 'HOME' ENTERED AT 11:26:00 ON 05 FEB 2004)

     FILE 'STNGUIDE' ENTERED AT 11:26:03 ON 05 FEB 2004

     FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 11:26:57 ON 05 FEB 2004
L1          2857 S CETP
L2           464 S L1 AND POLYMORPHISM?
L3           403 S L2 AND CHOLESTEROL
L4           255 S CETP (3A) (POLYMORPHISM? OR SNP?)
L5            75 S L4 (6A) HDL
L6            39 DUP REM L5 (36 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 11:32:19 ON 05 FEB 2004
L7             0 S L1 AND 307

     FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 11:54:00 ON 05 FEB 2004
L8             4 S L1 AND 307
L9             4 DUP REM L8 (0 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 11:55:52 ON 05 FEB 2004

     FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 11:58:28 ON 05 FEB 2004
L10            0 S L6 AND 565
L11            0 S L6 AND MSPI
L12            0 S L6 AND RSAI
L13           10 S L6 AND TAQI

     FILE 'STNGUIDE' ENTERED AT 12:03:49 ON 05 FEB 2004

     FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 12:10:38 ON 05 FEB 2004
L14           25 S L1 AND (MSP? OR RSA? OR 565)
L15           11 DUP REM L14 (14 DUPLICATES REMOVED)
L16            0 S L1 AND (565)
L17            2 S L1 AND (RSA?)
L18           25 S L1 AND MSP?
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ANSWER 4 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2002368222 MEDLINE
DOCUMENT NUMBER: 22108789 PubMed ID: 12116231
TITLE: Candidate genes involved in cardiovascular risk factors by a family-based association study on the island of Kosrae, Federated States of Micronesia.
AUTHOR: Han Zhihua; Heath Simon C; Shmulewitz Dvora; Li Wentian; Auerbach Steve B; Blundell Maude L; Lehner Thomas; Ott Jurg; Stoffel Markus; Friedman Jeffrey M; Breslow Jan L
CORPORATE SOURCE: Starr Center Human Genetics, Rockefeller University, New York, New York 10021, USA.
CONTRACT NUMBER: DK56208 (NIDDK)
GM07982 (NIGMS)
GM58757-01 (NIGMS)
HG00008 (NHGRI)
HL33714-17 (NHLBI)
SOURCE: AMERICAN JOURNAL OF MEDICAL GENETICS, (2002 Jul 1) 110 (3) 234-42.
Journal code: 7708900. ISSN: 0148-7299.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020713
Last Updated on STN: 20021010
Entered Medline: 20021008

AB Altered plasma levels of lipids and lipoproteins, obesity, hypertension, and diabetes are major risk factors for atherosclerotic cardiovascular disease. To identify genes that affect these traits and disorders, we looked for association between markers in candidate genes (apolipoprotein AII (apo AII), apolipoprotein AI-CIII-AIV gene cluster (apo AI-CIII-AIV), apolipoprotein E (apo E), cholesteryl ester transfer protein (**CETP**), cholesterol 7alpha-hydroxylase (CYP7a), hepatic lipase (HL), and microsomal triglyceride transfer protein (MTP)) and known risk factors (triglycerides (Tg), total cholesterol (TC), apolipoprotein AI (apo AI), apolipoprotein AII (apo AII), apolipoprotein B (apo B), body mass index (BMI), blood pressure (BP), leptin, and fasting blood sugar (FBS) levels.) A total of 1,102 individuals from the Pacific island of Kosrae were genotyped for the following markers: Apo AII/**MspI**, Apo CIII/SstI, Apo AI/XmnI, Apo E/HhaI, **CETP**/TaqIB, CYP7a/BsaI, HL/DraI, and MTP/HhpI. After testing for population stratification, family-based association analysis was carried out. Novel associations found were: 1) the apo AII/**MspI** with apo AI and BP levels, 2) the CYP7a/BsaI with apo AI and BMI levels. We also confirmed the following associations: 1) the apo AII/**MspI** with Tg level; 2) the apo CIII/SstI with Tg, TC, and apo B levels; 3) the Apo E/HhaI E2, E3, and E4 alleles with TC, apo AI, and apo B levels; and 4) the **CETP**/TaqIB with apo AI level. We further confirmed the connection between the apo AII gene and Tg level by a nonparametric linkage analysis. We therefore conclude that many of these candidate genes may play a significant role in susceptibility to heart disease.

L18 ANSWER 9 OF 25 MEDLINE on STN
ACCESSION NUMBER: 95341195 MEDLINE
DOCUMENT NUMBER: 95341195 PubMed ID: 7616125
TITLE: Polymorphisms at the apoB, apoA-I, and cholesteryl ester transfer protein gene loci in patients with gallbladder disease.
AUTHOR: Juvonen T; Savolainen M J; Kairaluoma M I; Lajunen L H; Humphries S E; Kesaniemi Y A
CORPORATE SOURCE: Department of Surgery, University of Oulu, Finland.
SOURCE: JOURNAL OF LIPID RESEARCH, (1995 Apr) 36 (4) 804-12.

Journal code: 0376606. ISSN: 0022-2275.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950905
Last Updated on STN: 19950905
Entered Medline: 19950818

AB Alterations in lipoprotein levels are reported to be related to an increased risk of gallstones. Plasma lipid metabolism is regulated by a number of proteins that are polymorphic in the population. The present research was designed to investigate the association between the polymorphisms of these proteins and the presence of various gallbladder diseases. Restriction fragment length polymorphisms (RFLPs) of apolipoprotein B (XbaI, EcoRI), apolipoprotein A-I (PstI, **MspI**), and cholesteryl ester transfer protein (**CETP**) (EcoNI, TaqIA, TaqIB) genes were examined in a series of 210 cholecystectomy patients operated on for symptomatic gallbladder disease and in 92 healthy controls. The patients were categorized into four groups according to the type of gallstones and the presence or absence of cholesterolosis. The distribution of **CETP** TaqIB polymorphism in the patients with cholesterol gallstones differed significantly from that in the controls, with the B1B1 jects (39.7%) (P = 0.036). The patients with both cholesterol and non-cholesterol stones had lower high density lipoprotein (HDL)-cholesterol levels than the control subjects. However, the most distinct difference was found in the gallstone patients with the B2B2 genotype (P = 0.006). The frequency of the X1X1 genotype of the apolipoprotein B XbaI polymorphism was markedly higher in the patients with acalculous cholesterolosis (48.9%) or cholesterolosis with stones (58.1%) than in the gallstone patients with cholesterol stones (27.2%) or with non-cholesterol stones (34.1%) (P = 0.002). The present data suggest that **CETP** gene polymorphism may ba associated with cholesterol gallstone disease, probably in combination with some additional factor that reduces the plasma HDL cholesterol concentration, especially in TaqIB B2B2 genotype.(ABSTRACT TRUNCATED AT 250 WORDS)

L18 ANSWER 10 OF 25 MEDLINE on STN
ACCESSION NUMBER: 95120902 MEDLINE
DOCUMENT NUMBER: 95120902 PubMed ID: 7820935
TITLE: DNA polymorphisms at the locus for human cholesteryl ester transfer protein (**CETP**) are associated with macro- and microangiopathy in non-insulin-dependent diabetes mellitus.
AUTHOR: Ukkola O; Savolainen M J; Salmela P I; von Dickhoff K; Kesaniemi Y A
CORPORATE SOURCE: Department of Internal Medicine, University of Oulu, Finland.
SOURCE: CLINICAL GENETICS, (1994 Sep) 46 (3) 217-27.
Journal code: 0253664. ISSN: 0009-9163.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502
ENTRY DATE: Entered STN: 19950223
Last Updated on STN: 19950223
Entered Medline: 19950216

AB The effect of variation at the cholesteryl ester transfer protein (**CETP**) gene locus and in the apolipoprotein (apo) AI-CIII-AIV gene cluster on the susceptibility of individuals with non-insulin-dependent diabetes mellitus (NIDDM) to atherosclerotic vascular disease was studied in 136 male and 122 female patients with NIDDM. The prevalence of myocardial infarction was high (38%) in patients with the EcoNI genotype

2-2 of the **CETP** gene locus (= 2-2; subjects homozygous for the absence of the restriction site) compared with patients with the genotype 1-1 (= 1-1; subjects homozygous for the presence of the restriction site) (18%, p < 0.02). The prevalence of any evidence of coronary heart disease (CHD) (presence of ischaemic ECG changes or definite myocardial infarction) was high in 2-2 (73%) compared with the genotype 1-2 (= 1-2; heterozygous for the presence of the restriction site) (52%, p < 0.02) and genotype 1-1 (p = 0.06). CHD was more prevalent in men with 2-2 (70%) than in those with 1-1 (42%, p < 0.05), but in women no significant differences were found in the prevalences of CHD between the EcoNI genotypes. Neuropathy was more often present in the patients with 2-2 (31%) than in those with 1-1 (12%, p < 0.02) or 1-2 (14%, p < 0.01). Plasma total cholesterol and total- and VLDL-triglycerides were higher in women with the EcoNI genotype 1-1 than in those with the genotype 1-2. In men no significant differences in plasma lipids were found. In addition, the prevalence of cerebrovascular disease was high (21%) in the patients with the genotype 1-1 of the TaqIB polymorphism compared with the genotype 2-2 (6%, p < 0.02). None of the alleles defined by four polymorphisms in the apo AI-CIII-AIV gene region were associated with an increased risk for macroangiopathy. The PstI polymorphism had an effect on plasma triglyceride levels. At the **CETP** locus one pair of loci (TaqIB and EcoNI) and three pairs of loci at the apo AI-CIII-AIV gene cluster (SacI and **MspI**, SacI and PvuII and **MspI** and PvuII) showed significant allelic association. In conclusion, the variation of **CETP** locus modulates the risk for diabetic complications in patients with NIDDM and the effect seems to be different between men and women. In contrast, the AI-CIII-AIV gene cluster polymorphisms seem not to be related to the risk of CHD in NIDDM.(ABSTRACT TRUNCATED AT 400 WORDS)

L18 ANSWER 11 OF 25 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:551878 BIOSIS
DOCUMENT NUMBER: PREV200300554844
TITLE: Use of an array technology for profiling and comparing transcription factors activated by TNFalpha and PMA in HeLa cells.
AUTHOR(S): Jiang, Xin [Reprint Author]; Norman, Michael; Li, Xianqiang
CORPORATE SOURCE: Panomics, Inc., 2003 East Bayshore Road, Redwood City, CA, 94063, USA
xjiang@panomics.com
SOURCE: Biochimica et Biophysica Acta, (23 September 2003) Vol. 1642, No. 1-2, pp. 1-8. print.
ISSN: 0006-3002 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Nov 2003
Last Updated on STN: 26 Nov 2003

AB Multiple signal transduction pathways are generally triggered simultaneously by a single extracellular stimulus. As a result, multiple transcription factors (TFs) can be activated downstream to mediate the inducible expression of target genes. Profiling the activation of all TFs will aid in the dissection of the numerous pathways of signal transduction. Tumor necrosis factor alpha (TNFalpha) and phorbol 12-myristate 13-acetate (PMA) mediate many biological functions, including cell proliferation and apoptosis, by stimulating signaling pathways. Two TFs, nuclear factor kappaB (NFkappaB) and activating factor 1 (AP1), have been identified as targets of both TNFalpha and PMA activation. Here, we describe the use of a protein/DNA array system to identify additional TFs activated by TNFalpha and PMA in HeLa cells. From a total of 150 targeted TFs, six-CREB, E2F, **CETP**/CRE, c-Rel, **MSP1**, and Pax6-were identified whose activities, like NFkappaB and AP1, were regulated by both TNFalpha- and PMA-induced pathways. Interestingly, the TF E47 was shown to be specifically activated by TNFalpha but was not affected by treatment with PMA. In addition, GATA, NF-E1, and ISRE were

shown to be specifically activated by PMA but not TNFalpha These findings suggest that TNFalpha and PMA both stimulate unique signaling pathways while mediating transcriptional activation through common pathways.

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L Number	Hits	Search Text	DB	Time stamp
1	175	cetp	USPAT	2004/02/05 12:23
3	17	cetp and (polymorphism$ or snp$)	USPAT	2004/02/05 12:23
2	3	cetp same (polymorphism$ or snp$)	USPAT	2004/02/05 12:23
4	18	cetp same (polymorphism$ or snp$)	USPAT; US-PGPUB; DERWENT	2004/02/05 12:24

*118470 CHOLESTERYL ESTER TRANSFER PROTEIN, PLASMA; CETP

Alternative titles; symbols

LIPID TRANSFER PROTEIN I

TABLE OF CONTENTS

Database Links

MEDLINE | Protein | DNA | HGMD | LocusLink | Gene Map | GDB | Nomenclature

Gene Map Locus: 16q21

Note: pressing the symbol will find the citations in MEDLINE whose text most closely matches the text of the preceding OMIM paragraph, using the Entrez MEDLINE neighboring function.

TEXT

DESCRIPTION

The transfer of insoluble cholesteryl esters among lipoprotein particles is a vital step in normal cholesterol homeostasis. One of the steps in this process is the transfer of cholesteryl esters by cholesteryl ester transfer protein (CETP).

CLONING

Using a partial amino acid sequence from purified CETP, Drayna et al. (1987) cloned and sequenced cDNA encoding CETP from a human liver library. They used the sequenced cDNA to

detect CETP mRNA in a number of human tissues. CETP is also known as lipid transfer protein I (Day et al., 1994).

GENE FUNCTION

Because the role of CETP in atherosclerosis remained unclear, Okamoto et al. (2000) attempted to develop a potent, specific CETP inhibitor. One inhibitor, JTT-705, forms a disulfide bond with CETP and increases high density lipoprotein (HDL) cholesterol, decreases non-HDL cholesterol, and inhibits the progression of atherosclerosis in rabbits. These observations suggested that CETP may be atherogenic in vivo and that JTT-705 may be a potential antiatherogenic drug.

GENE STRUCTURE

Oliveira et al. (1996) used transgenic mice to map the cis-acting sequences of the CETP gene. They localized a dietary cholesterol positive response element to the interval between -370 bp and -138 bp in the 5-prime proximal promoter region. Oliveira et al. (1996) found that more distal 5-prime promoter regions are required for tissue-specific expression in the liver, spleen, small intestine, adrenal gland, and other tissues.

MAPPING

Sparkes et al. (1987) used a CETP probe against DNA from a human/mouse somatic cell hybrid panel to assign the CETP gene to chromosome 16. In situ hybridization of the same probe to metaphase chromosomes regionalized the gene to 16q21. See also Lusis et al. (1987). This contributes a new marker for chromosome 16 inasmuch as RFLPs of this gene have been reported (Drayna and Lawn, 1987).

MOLECULAR GENETICS

Kondo et al. (1989) demonstrated an association between 1 allele of the CETP locus, as demonstrated by a TaqI polymorphism, and plasma apoA-I concentrations. The effect of the CETP alleles was limited to nonsmokers in this study.

In 3,469 men of Japanese ancestry in the Honolulu Heart Program, Zhong et al. (1996) found a high prevalence of 2 different CETP gene mutations: 5.1% for D442G (118470.0002) and 0.5% for the G-to-A substitution in the intron 14 donor site (118470.0001). The mutations were associated with decreased CETP (-35%) and increased HDL cholesterol levels (+10% for D442G) (see 607322). However, the overall prevalence of definite coronary heart disease was 21% in men with mutations and 16% in men without mutations.

HDL cholesterol concentration is inversely related to the risk of coronary artery disease. CETP has a central role in the metabolism of this lipoprotein and might therefore alter the susceptibility to atherosclerosis. For this reason, Kuivenhoven et al. (1998) studied the DNA of 807 men with angiographically documented coronary atherosclerosis for the presence of a polymorphism in the CETP gene. The specific polymorphism studied was a restriction polymorphism TaqIB in intron 1

of the CETP gene (Kuivenhoven et al., 1997). The TaqIB polymorphism had been shown to be associated with an effect on lipid-transfer activity (Hannuksela et al., 1994) and on HDL cholesterol concentrations (Freeman et al., 1994). The presence of the DNA variation was referred to as B1 and its absence as B2. All 807 patients in the study participated in a cholesterol-lowering trial designed to induce the regression of coronary atherosclerosis and were randomly assigned to treatment with either pravastatin or placebo for 2 years. The B1 variant of CETP was associated with both higher plasma CETP concentrations and lower HDL cholesterol concentrations. In addition, Kuivenhoven et al. (1998) observed a significant dose-dependent association between this marker and the progression of coronary atherosclerosis in the placebo group. This association was abolished by pravastatin. Pravastatin therapy slowed the progression of coronary atherosclerosis in B1B1 carriers but not in B2B2 carriers. This common DNA variant appeared to predict whether men with coronary artery disease will benefit from treatment with pravastatin to delay the progression of coronary atherosclerosis. In the total cohort, the B1 and B2 alleles were found at frequencies of 0.594 and 0.406, respectively. The observed frequencies were in Hardy-Weinberg equilibrium.

Fumeron et al. (1995) found that alcohol intake modulates the effect of the TaqIB polymorphism on plasma HDL and the risk of myocardial infarction. They found that HDL cholesterol was increased in subjects with the B2B2 genotype only when they ingested at least 25g of alcohol per day. In that study, the cardio-protective effect of the B2B2 CETP genotype was restricted to subjects who consumed the highest amounts of alcohol. Dullaart et al. (1997), in a study of patients with insulin-dependent diabetes, demonstrated that the ratio of very low density lipoprotein cholesterol plus LDL cholesterol to HDL cholesterol fell in response to a linoleic acid-enriched, low-cholesterol diet in B1B1 homozygotes but not in B1B2 heterozygotes.

Durlach et al. (1999) studied the B polymorphism of the CETP gene in 406 type II diabetic (125853) patients aged 59.5 +/- 10.8 years, with a body mass index of 28.9 +/- 5.3 kg/m2, and glycosylated hemoglobin of 8.2 +/- 1.9%. Patients were separated into 2 groups, 231 males (78 B1B1, 108 B1B2, and 45 B2B2) and 175 females (48 B1B1, 94 B1B2, and 33 B2B2), and were compared on the basis of their lipid parameters (total cholesterol, triglycerides, HDL cholesterol (HDLC), APOA1 (107680)/APOB (107730), and LDL cholesterol) and their micro- and macrovascular complications. HDLC was significantly higher in men with the B2B2 genotype, together with a lower incidence of coronary heart disease. Women displayed a higher HDLC than men and an equally high incidence of coronary heart disease in B2 homozygotes as in other genotypes. The authors concluded that in type II diabetic patients, the B polymorphism exerts a modulating role in males only and that this may contribute to the loss of macrovascular protection in type II diabetic females.

Altshuler et al. (1998) expressed caution concerning the interpretation of studies of association between allelic variants and common diseases. The 2 issues they raised in urging caution were, first, population admixture, which can cause an artificial association if a study includes genetically distinct subpopulations, one of which coincidentally displays a higher frequency of disease and allelic variants. Consideration of the ethnic backgrounds of subjects and the use of multiple, independent populations can help avoid this problem. The most persuasive tests, however, involve family-based controls such as the transmission disequilibrium test. In this test, if a given allele contributes to disease, then the probability that an affected person has inherited the allele from a heterozygous parent should vary from the expected mendelian ratio of 50:50; the association of a neutral polymorphism due to admixture displays no such deviation. A second source of concern is multiple-hypothesis testing, aggravated by publication bias. Authors who test a single genetic variant for an association with a single phenotype base statistical thresholds for significance on a

single hypothesis. However, many laboratories search for associations using different variants. Each test represents an independent hypothesis, but only positive results are reported, leading to an overestimate of the significance of any positive associations. Statistical correction for multiple testing is possible, but the application of such thresholds result in loss of statistical power.

ANIMAL MODEL

The acceleration of atherosclerosis by polygenic (essential) hypertension is well recognized in humans; however, the lack of an animal model that simulates the human disease hinders elucidation of pathogenic mechanisms. Herrera et al. (1999) reported a transgenic atherosclerosis-polygenic hypertension model in Dahl salt-sensitive hypertensive rats that overexpress the human cholesteryl ester transfer protein. Male transgenic rats fed regular rat chow showed age-dependent severe combined hyperlipidemia, atherosclerotic lesions, myocardial infarctions, and decreased survival. These findings differed from various mouse atherosclerosis models, demonstrating the necessity of complex disease modeling in different species. The data demonstrated that CETP can be proatherogenic.

To determine the relationship between apolipoprotein C-I (APOC1; 107710) and CETP, Gautier et al. (2002) crossed transgenic mice expressing human CETP with Apoc1 null mice. The HDLs of these crosses contained 50% less cholesteryl esters and showed a decreased cholesteryl ester-to-triglyceride ratio. The mean apparent diameter of LDLs from these mice was also significantly reduced. In vitro, purified Apoc1 inhibited cholesteryl ester exchange when added to either total plasma or to reconstituted HDL-free mixtures. Gautier et al. (2002) concluded that APOC1 is a specific inhibitor of CETP.

ALLELIC VARIANTS
(selected examples)

.0001 CETP DEFICIENCY [CETP, IVS14DS, G-A, +1]

Using monoclonal antibodies, Brown et al. (1989) showed that 2 Japanese sibs with markedly increased and enlarged HDL had CETP deficiency (607322). They were homozygous for a point mutation in the 5-prime splice donor site of intron 14 of the CETP gene. The mutation was a change of the strictly conserved G-T intron splice donor to A-T. The family illustrates the key role of CETP in HDL metabolism. Plasma CETP catalyzes the transfer of cholesteryl esters from HDL to other lipoproteins.

Inazu et al. (1990) identified the same CETP mutation in 4 additional Japanese families with increased HDL levels, including a family reported by Saito (1984) with unusual longevity and increased HDL levels (see hyperalphalipoproteinemia; 143470). The lipoprotein phenotype of CETP deficiency, which is characterized by both increased levels of HDL and decreased levels of low density lipoprotein (LDL), appeared to have strong antiatherogenic potential. CETP deficiency appears to be a frequent cause of increased HDL levels in the population of Japan, possibly because of founder effect. Familial hypobetalipoproteinemia (107730.0006) is another antiatherogenic mutation.

The G-to-A mutation was found in homozygous state in 2 patients by Yamashita et al. (1990).

Heterozygosity for the mutation was found in 2 other probands who totally lacked CETP and whose lipoprotein patterns were similar to those of the 2 homozygotes. They were presumably compound heterozygotes. Compound heterozygotes associated with hyperalphalipoproteinemia are described in 118470.0002.

.0002 CETP DEFICIENCY [CETP, ASP442GLY]

Takahashi et al. (1993) reported 2 unrelated, healthy females who were heterozygous for a G-to-A transition in exon 15 of the CETP gene, resulting in a substitution of gly for asp at amino acid 442. Both women had 3-fold increases in HDL concentrations and markedly decreased plasma CETP mass and activity (see 607322), suggesting that the mutation has dominant effects on CETP and HDL in vivo. The dominant effect of the CETP mutation raises the possibility that the active species of CETP is multimeric. Inazu et al. (1994) found a heterozygote frequency of 7% for the D442G mutation in a sample of 236 Japanese men. The heterozygote frequency of the IVS14 splice mutation (118470.0001) was estimated to be 2%. The 2 mutations accounted for about 10% of the total variance of HDL cholesterol values in the Japanese population studied.

Akita et al. (1994) found either the IVS14 splice mutation or the D442G mutation, or both, in 44 out of 226 unrelated patients with hyperalphalipoproteinemia (143470). The IVS14 mutation was found in 15 patients, including 4 compound heterozygotes for the 2 mutations; D442G was identified in 33, including the 4 compound heterozygotes. Allelic frequencies in the general population for the IVS14 and the D442G mutations were 0.81% and 4.62%, respectively. The IVS14 mutation was responsible for a more severe form of hyperalphalipoproteinemia.

Among 117 Japanese hyperalphalipoproteinemic subjects without the intron 14 splice defect (118470.0001), Sakai et al. (1995) found 3 homozygotes (2.5%) and 34 heterozygotes (29.1%) for the D442G mutation. These results suggested that this mutation is as common as the intron 14 splice defect in Japanese hyperalphalipoproteinemic subjects. One of the homozygotes was the patient previously described by Takahashi et al. (1993) as having hyperalphalipoproteinemia with corneal opacity and coronary heart disease. They had previously thought that this patient was heterozygous.

.0003 CETP DEFICIENCY [CETP, IVS14DS, INS T, +3]

Inazu et al. (1994) screened Japanese subjects with high density lipoprotein cholesterol levels in excess of 100 mg/dl by PCR single-strand conformation polymorphism analysis of the CETP gene. They found a novel intron 14 splice donor site mutation caused by a T insertion at position +3 from the exon 14/intron 14 boundary. The phenotype of a genetic compound heterozygote for this mutation and the IVS14 splice mutation (118470.0001) was similar to that of the homozygote for the latter mutation: no detectable CETP and markedly increased HDL cholesterol levels (see 607322).

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terry : 7/30/1998
dholmes : 5/12/1998
dholmes : 5/12/1998
mark : 9/19/1996
marlene : 8/15/1996
mark : 6/29/1995
carol : 11/29/1994
mimadm : 6/25/1994
carol : 10/29/1993
carol : 10/28/1992
carol : 4/28/1992

ALLELIC VARIANTS

(selected examples)

- 0001 : CETP DEFICIENCY
  - Mutation : CETP, IVS14DS, G-A, +1
- 0002 : CETP DEFICIENCY
  - Mutation : CETP, ASP442GLY
- 0003 : CETP DEFICIENCY
  - Mutation : CETP, IVS14DS, INS T, +3